UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,096	03/06/2001	Carl-Magnus A. Andersson	015185/027 2568	2737

7590 04/25/2002

Pillsbury Winthrop LLP
Intellectual Property Group
50 Fremont Street
San Francisco, CA 94105-2228

EXAMINER
PATEL, SUDHAKER B

ART UNIT	PAPER NUMBER
1624	8

DATE MAILED: 04/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/800,096	Carl-Magnus A. Andersson et al
Examiner	**Art Unit**
Sudhaker Patel	1624

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 29, 2002*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-52* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-52* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Applicants' communication paper #7 dated 3/29/02 is acknowledged.

1. Election/Restriction:

Because applicants did not distinctly and specifically point out the supposed errors in the restriction/election requirement, the election has been treated as an election without traverse(MPEP 818.03(a)).

Applicants have elected Group I, claims (in part) 1-52, drawn to compounds, simple compositions, and a method of use for generic Formula I of claim 1 wherein W = O; Z = piperidine, and species of Example 127(= 4-Methylbenzyl)-N-(1-methylpiperidine-4-yl)-'N'-(4-methoxybenzyl)-carbamide. Since claims link with other inventions, this application will be examined bearing in mind the subject matter of Group I and species of Example 127 as elected by the applicants only. Applicants are urged to limit the scope of the claims to elected subject matter in reply to this Office Action after checking the claim dependency.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-5,6-7,8-14,15-35,36-49,50-52 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact

terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

(A). Claims 1,8,14, and claims dependent on these claims recite " aryl, aralkyl, heteraralkyl, heteroaryl for variables R, Ar1, Ar2". Specification on page 10(lines 33-34),page 11 (lines 1-35) provide preferred examples for each terms, but the claims remain silent.

The term "heteroaryl" as defined on page 11 line 20 includes aromatic C2-6 cyclic groups containing O, S, or up to four N atoms, or combination of one O or S atom with up to two N atoms. It is difficult to read C2 or C3-C4 aromatic cyclic rings having different heteroatoms.

Applicants are reminded that although the claims are interpreted in light of the specification, critical limitations from the specification cannot be read into the claims (see, e.g., In re Van Guens, 988 F.2d 1181, 26 PSPG2d 1057 (Ded. Cir. 1991)). Accordingly, without the recitation of all these critical limitations, the claims do not adequately define the instant invention.

(B). Specification on page 12 line 24 recites " X ". It is not clear as to what applicants desire to describe. Correction is requested.

(C). Claims 1-5 ,7,8-12 all recite compounds where as claim 6, 13, recite Formula (II) as salt. Claim 14 reciting Formula I compounds(see page 140, lines 8/9) also recited their salt(s), ester(s) or "prodrug) (see page 141, lines 8/9). It is suggested to include the " salt, prodrug" in claim 1.

(D). Independent Claim 14 recites " ester or prodrug". It is not very clear as to difference between these two terms. Claims reads as "prodrug " is different than "ester.

On page 29, lines 4-5 recites"resolution of compounds by formation of esters or amides". Clarifications is requested.

(E). Claim 7 recites compounds of claim 1 which has Formula I. However, claim 13 recited claim 7, having a Formula (II). Therefore, it is difficult to understand what applicants want to say. Correction is required.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5,8-14,15-35,36-49,50-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

(I). **HOW TO MAKE:** The specification fails to enable the preparation of the claimed compounds. Most of the compounds of examples recited have Z = piperidine; Ar1/ Ar2 = substituted phenyl, but not Z = 9-membered azabicyclic core connected from the middle (figure 7 of line 10 in claim 1); R = substituted benzoisoxazolyl; Ar1 = pyrido-fused triazine (6-6 membered heterocycle);Ar2 = pyrido-thiomorpholine(6-6 membered heterocycle); connecting chain = Y2-Y1-N(Z)-CO-X1-X2- (wherein X1 = NH;X2 = methylene;Y1 = ethylene; Y2 =

N(lower alkyl). In the specification on pages 34,35 the schemes teaches making of derivatives of monocyclic amines from ketones or their procurement from commercial source, but remain silent for the substituted azabicyclo-compounds. Sources of certain starting materials and making of piperidine type monoazacyclic compounds are given, but not related to claimed structures noted above.

In view of the lacks of direction provided in the specification regarding starting materials, the lack of working examples and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

The starting material sources necessary to obtain the instant compounds must have been available as of the filing date in order to provide an enabling disclosure. See In re Howarth, 654 F.2d 103, 210 USPQ 689 (CCPA 1981); Ex parte Moersch, 104 USPQ 122 (POBA 1954). Applicants should show that the sources of these starting materials was common knowledge or readily available at the time of filling.

(II). HOW TO USE: The specification fails to enable one skilled in the art to use the claimed compounds having activity which could be signaling activity, constitutive activity or activity associated with serotonin receptor activation, and at the same time the compounds could be used for a method for identifying a genetic polymorphism predisposing a subject to being responsive to one or more of the compounds of claim 1, comprising; administering to a subject a therapeutically effective amount of the compound; measuring the response of said subject to said

compound, thereby identifying a responsive subject having an ameliorated disease condition associated with a monoamine receptor not limited to treating thrombosis only but also schizophrenia, migraine, hypertension, vasospasm, ischemia, depression, anxiety, sleep disorders, appetite disorders and others as claimed herein. Extensive testing is provided at pages 118-128, however, not all assay results(see pages 122-123 for Example 138 for species of Example 127/47AKU-44 are disclosed. Table 4 on page 120 recited Percent efficacy(range 58-129); pIC50(range 7.7-9.8). These tests serve as the vehicle for preliminary screening of the compounds which will require further testing. All the compounds actually tested are structurally different from the claimed compounds such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the instantly claimed compounds. Furthermore, this area of receptor interactions is highly structure specific and unpredictable, as evidenced by the wide range of results obtained for the tested compounds. Receptor activity is generically an unpredictable and highly structure specific area.

In view of the breath of the claims, the chemical nature of the invention, the unpredictability of monoamine receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for treating disease conditions related to vasospasm, depression, hypertension, schizophrenia and other as recited herein. There's no reasonable likelihood of success in the use of the claimed compound

for the disclosed activity and resulting method of treating as well as method of indentifying a genetic polymorphism as recited herein.

Applicants' attention is drawn to MPEP 806.05(h) which provides for one method of use to be examined with the elected compounds. A broad disclosure of utility as in the cited claims 15-52 can not be deemed in compliance with 35 U.S.C. 112, first paragraph.

Therefore, applicants should limit the method claim to a sole "specific utility", and provide necessary supporting evidence for the same by appropriate tests which should include the corresponding reference compounds.

4. *Conclusion*

Allowable Subject Matter

Compounds, compositions claims 1-14, method of use claims involving use for thrombosis, migraine, appetite disorders would be allowable, provided applicants resolve the issues raised in this action.

The closest prior art deem to be Maduskuie et al (WO9738984 dated 10/23/1997) disclosing compound CAS RN# 198823-73-3 having a core: CLCH2-phenyl-CH2-N(substituted piperidine)-CO-NH-Phenyl-CN which has activity related to factor Xa inhibitors. There's no suggestion or indication arrive at the instant compounds by way of motivation.

This application has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is, therefore, requested in promptly correcting any errors of which they may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker Patel,D.Sc.Tech. whose telephone number is (703) 308 4709.

The examiner can normally be reached on Monday thru' Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Dr.Mukund Shah can be reached at (703) 308 4716.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

Any inquiry of general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308 1235.

Mukund J. Shah

MUKUND J. SHAH
SUPERVISORY PATENT EXAMINER
GROUP 1600

S.p.
April 19, 2002.